AHRQ Healthcare Horizon Scanning System – Potential High-Impact Interventions Report

Priority Area 03: Cardiovascular Disease

Prepared for:
Agency for Healthcare Research and Quality
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Contract No. HHSA290201000006C

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June 2014

Statement of Funding and Purpose

This report incorporates data collected during implementation of the Agency for Healthcare Research and Quality (AHRQ) Healthcare Horizon Scanning System by ECRI Institute under contract to AHRQ, Rockville, MD (Contract No. HHSA290201000006C). The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

This report's content should not be construed as either endorsements or rejections of specific interventions. As topics are entered into the System, individual topic profiles are developed for technologies and programs that appear to be close to diffusion into practice in the United States. Those reports are sent to various experts with clinical, health systems, health administration, and/or research backgrounds for comment and opinions about potential for impact. The comments and opinions received are then considered and synthesized by ECRI Institute to identify interventions that experts deemed, through the comment process, to have potential for high impact. Please see the methods section for more details about this process. This report is produced twice annually and topics included may change depending on expert comments received on interventions issued for comment during the preceding 6 months.

A representative from AHRQ served as a Contracting Officer's Technical Representative and provided input during the implementation of the horizon scanning system. AHRQ did not directly participate in horizon scanning, assessing the leads for topics, or providing opinions regarding potential impact of interventions.

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None of the individuals compiling this information has any affiliations or financial involvement that conflicts with the material presented in this report.

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Suggested citation: ECRI Institute. AHRQ Healthcare Horizon Scanning System Potential High-Impact Interventions: Priority Area 03: Cardiovascular. (Prepared by ECRI Institute under Contract No. HHSA290201000006C.) Rockville, MD: Agency for Healthcare Research and Quality. June 2014. http://effectivehealthcare.ahrq.gov/index.cfm/

Preface

The purpose of the AHRQ Healthcare Horizon Scanning System is to conduct horizon scanning of emerging health care technologies and innovations to better inform patient-centered outcomes research investments at AHRQ through the Effective Health Care Program. The Healthcare Horizon Scanning System provides AHRQ a systematic process to identify and monitor emerging technologies and innovations in health care and to create an inventory of interventions that have the highest potential for impact on clinical care, the health care system, patient outcomes, and costs. It will also be a tool for the public to identify and find information on new health care technologies and interventions. Any investigator or funder of research will be able to use the AHRQ Healthcare Horizon Scanning System to select potential topics for research.

The health care technologies and innovations of interest for horizon scanning are those that have yet to diffuse into or become part of established health care practice. These health care interventions are still in the early stages of development or adoption, except in the case of new applications of already-diffused technologies. Consistent with the definitions of health care interventions provided by the Institute of Medicine and the Federal Coordinating Council for Comparative Effectiveness Research, AHRQ is interested in innovations in drugs and biologics, medical devices, screening and diagnostic tests, procedures, services and programs, and care delivery.

Horizon scanning involves two processes. The first is identifying and monitoring new and evolving health care interventions that are purported to or may hold potential to diagnose, treat, or otherwise manage a particular condition or to improve care delivery for a variety of conditions. The second is analyzing the relevant health care context in which these new and evolving interventions exist to understand their potential impact on clinical care, the health care system, patient outcomes, and costs. It is NOT the goal of the AHRQ Healthcare Horizon Scanning System to make predictions on the future use and costs of any health care technology. Rather, the reports will help to inform and guide the planning and prioritization of research resources.

We welcome comments on this Potential High-Impact Interventions report. Send comments by mail to the Task Order Officer named in this report to: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to: effectivehealthcare@ahrq.hhs.gov.

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Background

Horizon scanning is an activity undertaken to identify technological and system innovations that could have important impacts or bring about paradigm shifts. In the health care sector, horizon scanning pertains to identification of new (and new uses of existing) pharmaceuticals, medical devices, diagnostic tests and procedures, therapeutic interventions, rehabilitative interventions, behavioral health interventions, and public health and health promotion activities. In early 2010, the Agency for Healthcare Research and Quality (AHRQ) identified the need to establish a national Healthcare Horizon Scanning System to generate information to inform comparative-effectiveness research investments by AHRQ and other interested entities. AHRQ makes those investments in 14 priority areas. For purposes of horizon scanning, AHRQ's interests are broad and encompass drugs, devices, procedures, treatments, screening and diagnostics, therapeutics, surgery, programs, and care delivery innovations that address unmet needs. Thus, we refer to topics identified and tracked in the AHRQ Healthcare Horizon Scanning System generically as "interventions." The AHRQ Healthcare Horizon Scanning System implementation of a systematic horizon scanning protocol (developed between September 1 and November 30, 2010) began on December 1, 2010. The system is intended to identify interventions that purport to address an unmet need and are up to 3 years out on the horizon and then to follow them up to 2 years after initial entry into the health care system. Since that implementation, review of more than 18,000 leads about potential topics has resulted in identification and tracking of about 2,000 topics across the 14 AHRQ priority areas and 1 cross-cutting area; about 550 topics are being actively tracked in the system.

Methods

As part of the Healthcare Horizon Scanning System activity, a report on interventions deemed as having potential for high impact on some aspect of health care or the health care system (e.g., patient outcomes, utilization, infrastructure, costs) is aggregated twice a year. Topics eligible for inclusion are those interventions expected to be within 0–3 years of potential diffusion (e.g., in phase III trials or for which some preliminary efficacy data in the target population are available) in the United States or that have just begun diffusing and that have completed an expert feedback loop.

The determination of impact is made using a systematic process that involves compiling information on topics and issuing topic drafts to a small group of various experts (selected topic by topic) to gather their opinions and impressions about potential impact. Those impressions are used to determine potential impact. Information is compiled for expert comment on topics at a granular level (i.e., similar drugs in the same class are read separately), and then topics in the same class of a device, drug, or biologic are aggregated for discussion and impact assessment at a class level for this report. The process uses a topic-specific structured form with text boxes for comments and a scoring system (1 minimal to 4 high) for potential impact in seven parameters. Participants are required to respond to all parameters.

The scores and opinions are then synthesized to discern those topics deemed by experts to have potential for high impact in one or more of the parameters. Experts are drawn from an expanding database ECRI Institute maintains of approximately 150 experts nationwide who were invited and agreed to participate. The experts comprise a range of generalists and specialists in the health care sector whose experience reflects clinical practice, clinical research, health care delivery, health business, health technology assessment, or health facility administration perspectives. Each expert uses the structured form to also disclose any potential intellectual or financial conflicts of interest

(COIs). Perspectives of an expert with a COI are balanced by perspectives of experts without COIs. No more than two experts with a possible COI are considered out of a total of the five to eight experts who are sought to provide comment for each topic. Experts are identified in the system by the perspective they bring (e.g., clinical, research, health systems, health business, health administration, health policy).

The topics included in this report had scores *and/or* supporting rationales at or above the overall average for all topics in this priority area that received comments by experts. Of key importance is that topic scores alone are not the sole criterion for inclusion—experts' rationales are the main drivers for the designation of potentially high impact. We then associated topics that emerged as having potentially high impact with a further subcategorization of "lower," "moderate," or "higher" within the high-impact-potential range. As the Healthcare Horizon Scanning System grows in number of topics on which expert opinions are received and as the development status of the interventions changes, the list of topics designated as having potentially high impact is expected to change over time. This report is being generated twice a year.

For additional details on methods, please refer to the full AHRQ Healthcare Horizon Scanning System Protocol and Operations Manual published on AHRQ's Effective Health Care Web site.

Results

The table below lists the 10 topics for which (1) preliminary phase III data for drugs, phase II (or equivalent) data for devices and procedures, or some human data for off-label uses or programs were available; (2) information was compiled and sent for expert comment before May 15, 2014, in this priority area; *and* (3) we received five to eight sets of comments from experts between July 1, 2013, and May 23, 2014. (Fifty-one topics were being tracked in this priority area as of May 15, 2014.) We present six summaries on six topics (indicated below by an asterisk) that emerged as having potential for high impact on the basis of experts' comments. The material on interventions in this Executive Summary and report is organized alphabetically by disease state and then by interventions within that disease state. Readers are encouraged to read the detailed information on each intervention that follows the Executive Summary.

Priority Area 03: Cardiovascular

Topic	High-Impact Potential
1. Cardiac resynchronization therapy for heart failure with atrioventricular block	No high-impact potential; archived in horizon scanning system on basis of expert comments
2. Catheter-based renal denervation (Symplicity System) for treatment-resistant hypertension	No high-impact potential at this time; continue to track
3. * Lomitapide (Juxtapid) for treatment of homozygous familial hypercholesterolemia	Moderately high
4. * Percutaneous left atrial appendage occlusion (Watchman device) for prevention of atrial fibrillation–associated stroke	Moderately high
5. * Portable Freedom Driver for in-home support of the Total Artificial Heart	Lower end of the high-impact-potential range
6. * Subcutaneous Implantable Cardioverter-Defibrillator (S-ICD) for treatment of life-threatening ventricular tachyarrhythmias	Lower end of the high-impact-potential range
7. * Transcatheter aortic valve implantation (CoreValve) for treatment of severe aortic stenosis	High
8. * Transcatheter mitral valve repair (MitraClip) for treatment of mitral regurgitation	Moderately high

Topic	High-Impact Potential
9. Treprostinil diolamine (Orenitram) for treatment of pulmonary artery hypertension	No high-impact potential; archived in horizon scanning system on basis of expert comments
10. Wireless monitoring system (Champion) for management of heart failure	No high-impact potential; archived in horizon scanning system on basis of expert comments

Discussion

Research activity in all disease areas of the cardiovascular priority area is robust and addresses both novel and incremental innovations that could affect patient outcomes, shift care models, and affect costs and care delivery. Most of the innovations being tracked, as well as the innovations deemed by expert comments to have potential for high impact pertain to cardiovascular devices that provide support for end-stage heart failure (HF) or address valve problems, arrhythmias, stroke, and treatment-resistant hypertension. Only one pharmaceutical, lomitapide, was deemed as having potential for high impact.

The following four topics were eligible for consideration in this report, but deemed as having no potential for high impact on the basis of expert comments.

- **Cardiac resynchronization therapy for heart failure with atrioventricular block:** Cardiac resynchronization therapy with biventricular pacing devices is under development by Medtronic, Inc. (Minneapolis, MN). Atrioventricular block is typically treated with right ventricular pacing; however, ventricular dyssynchrony caused by right ventricular pacing is thought to adversely affect left ventricular function and geometry, so it may present problems in patients with existing cardiac dysfunction. Experts commenting on this topic saw no potential for high impact because of limited efficacy data that it would markedly improve patient health, a small affected patient population, and potential for adverse events. In light of experts' comments, this topic has been archived in the horizon scanning system.
- **Catheter-based renal denervation (Symplicity RDN System) for treatment-resistant hypertension:** The Symplicity RDN System (Medtronic) uses low-power radiofrequency energy delivered to renal artery nerves to deactivate sympathetic nerves in an attempt to reduce hypertension. In January 2014, the manufacturer announced that its pivotal randomized controlled trial (RCT), the SYMPLICITY HTN-3 trial, did not meet its primary efficacy endpoint in reducing hypertension in patients with treatment-resistant disease. The manufacturer subsequently discontinued its SYMPLICITY HTN-4 trial for this patient population and announced on March 29, 2014, that it would perform additional analyses on the existing trial data and continue to develop the device. The device is marketed in Europe. We will continue to track this topic in the horizon scanning system.
- **Treprostinil diolamine (Orenitram) for treatment of pulmonary artery hypertension:** Treprostinil diolamine (United Therapeutics Corp., Silver Spring, MD) is a sustained-release oral prostacyclin intended for use early in the pulmonary artery hypertension (PAH) disease continuum. Treprostinil diolamine purportedly vasodilates pulmonary and systemic arterial vascular beds and inhibits platelet aggregation; it is intended as an add-on therapy to oral therapies. Experts commenting saw no potential for high impact because of availability of other pharmacotherapies to treat PAH. In light of experts' comments, this topic is being archived in the horizon scanning system.
- **Wireless monitoring system (Champion) for management of heart failure:** The Champion device (developed by CardioMEMS, Inc., Atlanta, GA, and acquired in June 2014 by St. Jude Medical, St. Paul, MN) was renamed CardioMEMS™ HF System and is a

self-contained, paper clip–size device placed in the pulmonary artery during a catheter-based procedure. A patient holds an external electronic module over the chest to wirelessly power the sensor and collect blood-pressure data using radiofrequency energy. The handheld unit then transmits data to the CardioMEMS Champion Web site, which a clinician monitors, thus enabling quick adjustments to medications and potentially reducing HF-related hospitalizations. The device received approval from the U.S. Food and Drug Administration (FDA) in May 2014. Experts commenting on this device noted that evidence comes from only a single RCT with short-term outcomes and that the technology has the possibility of serious side effects. Experts thought that conclusive evidence of a large, clinically significant impact on health outcomes or cost reductions was not available and that patients would need to be highly motivated to use the technology and comply with regular monitoring requirements. Thus, they saw little potential for high impact. In light of experts' comments, this topic is being archived in the horizon scanning system.

Here are the six interventions that expert commenters thought have potential for high impact. They are devices to treat arrhythmia, atrial fibrillation–associated stroke, HF, and cardiac valve disorders and a drug to treat a genetic disorder.

Arrhythmia

According to the American Heart Association (AHA), arrhythmias (abnormal heartbeats) are a major source of cardiovascular-related morbidity and mortality. Ventricular tachycardia (rapid heartbeat) and ventricular fibrillation (unsynchronized heartbeat) reduce the heart's pumping ability and can cause collapse, cardiac arrest, and sudden death. These conditions are believed to contribute to the more than 400,000 deaths from sudden cardiac arrest that occur in the United States each year. Numerous drugs and implantable devices exist to treat arrhythmias. Drugs for heart rhythm and rate control carry significant risks of adverse events, and available implantable devices often contraindicate certain procedures (e.g., magnetic resonance imaging [MRI]). Therefore, a significant unmet need exists for better and safer treatments for patients with forms of cardiac arrhythmia. Experts commented on one intervention with potential high impact in treating arrhythmia.

Subcutaneous Implantable Cardioverter-Defibrillator (S-ICD) for Treatment of Life-Threatening Ventricular Tachyarrhythmias

- **Key Facts:** Until the Subcutaneous Implantable Cardioverter-Defibrillator (S-ICD®) System (Boston Scientific Corp., Natick, MA) was FDA approved for marketing in September 2012, only implantable cardioverter-defibrillators (ICDs) that use implanted leads had been available. ICDs can prevent sudden cardiac death by treating ventricular tachyarrhythmias, but they had required implanting a transvenous lead in the heart. Complications are known to arise from leads over time, and procedures to remove faulty leads are often associated with serious morbidity and mortality. The S-ICD is intended to be a minimally invasive option that does not require electrode lead placement in or on the heart. Further, the device does not require imaging equipment for placement because the system components are designed to be positioned using only anatomic landmarks. According to FDA-approved product labeling, the device is approved for use only in patients who do not require a pacemaker or pacing therapy.

  In 2014, Lambiase and colleagues reported interim results from the EFFORTLESS postmarket observational study of patients receiving the S-ICD, which reported that S-ICD

implantation had low complication rates. Among the 456 treated patients, investigators reported complication-free rates of 97% and 94% at 30 and 360 days, respectively. At 360 days, the inappropriate shock rate was 7%, primarily attributed to oversensing of cardiac episodes.

The device cost is reported to be similar to that of conventional ICDs and the procedure purportedly takes less time to perform because it can be performed in an outpatient setting with no need for fluoroscopy, other imaging, or an electrophysiology laboratory. In coverage policies addressing conventional ICDs, several private, third-party payers describe the S-ICD as investigational or experimental and, therefore, deny coverage, despite FDA approval. Some payers noted a desire for more data showing that safety and efficacy is equivalent to transvenous ICDs. The American Medical Association Current Procedural Terminology has established category III codes for the S-ICD to enable tracking of use. The U.S. Centers for Medicare & Medicaid Services (CMS) has a national coverage determination for ICDs and criteria for coverage, but it does not mention the S-ICD system.

- **Key Expert Comments:** Experts were optimistic that this intervention has potential to improve patient health outcomes by reducing complications associated with lead-based ICDs that carry a high risk of morbidity and some mortality. Experts noted this device's potential to reduce inappropriate shocks compared with conventional ICDs. However, some experts suggested that this device's limited pacing capabilities could temper widespread diffusion and impact. Because the implantation procedure requires fewer resources and can be performed in an outpatient setting, this intervention could shift care delivery to a less-invasive setting and result in shorter hospital stays and cost savings compared with conventional ICD implantation.
- **Potential for High Impact:** Lower end of the potential high-impact range

Atrial Fibrillation–Associated Stroke

A serious complication of atrial fibrillation (AF) is ischemic stroke. Risks for ischemic stroke after all standard stroke risk factors are accounted for are four- to fivefold greater in patients with AF than in other individuals. Stroke risk is high in AF because thrombi form in the atria or, more commonly, in the left atrial appendage. A stroke results when a part of a thrombus breaks off into the systemic circulation and travels to the brain, blocking blood flow to an area there. Anticoagulant therapy is used in an attempt to prevent stroke in patients with AF; however it has been estimated that from 14% to 44% of patients with AF have bleeding risks that preclude them from taking anticoagulants. Additionally, the need for frequent monitoring, dosage adjustments, and dietary restrictions makes the standard anticoagulant therapy, warfarin, a less-than-optimal therapy with discontinuation rates estimated to be about 38% per year. Although newly approved anticoagulant alternatives to warfarin, (e.g., apixaban, dabigatran, rivaroxaban) eliminate the need for routine monitoring and dietary restrictions, these therapies have other drawbacks, including nonhemorrhagic side effects, potential for drug-drug interactions, and the fact that no antidote is available in the event of uncontrolled bleeding. Therefore, an unmet need exists for better and safer treatments for AF-associated stroke. Experts commented on one intervention with potential high impact in treating arrhythmia.

Percutaneous Left Atrial Appendage Occlusion (Watchman) for Prevention of AF-Associated Stroke

- **Key Facts:** The Watchman® LAA Closure Technology is a device that is implanted in the left atrial appendage (LAA) to occlude its opening and prevent thrombi from entering the

systemic circulation. The device may be an alternative to anticoagulant therapy to prevent stroke in patients with AF. The device was developed by Atritech (Minneapolis, MN), which Boston Scientific acquired in 2011. The device is limited to investigational use in the United States at this time. In December 2013, the Circulatory System Devices Panel of FDA's Medical Devices Advisory Committee voted 13-1 that benefits outweighed risks and to recommend marketing approval for the device to reduce the risk of embolic stroke in patients with AF. It was the second time the device had been considered by an FDA panel. In mid-June 2014, the company announced at an investor conference that FDA had just rendered a decision requiring the device to go before a third FDA advisory panel before a final decision could be made. The company now anticipates a decision in the first half of 2015. The device was Conformité Européene (CE) marked in 2005, allowing marketing in Europe, and it was commercialized outside the United States in 2009.

In February 2013, Reddy and colleagues reported results of a 2.3-year followup of primary efficacy from the PROTECT AF trial. Investigators observed primary efficacy event rates of 3.0% and 4.3% in the device and control groups, respectively. Primary safety events occurred in 5.5% per year in the device group compared with 3.6% per year in the control group. In March 2013, the manufacturer reported results from a confirmatory study requested by FDA. The PREVAIL trial evaluated safety and efficacy of the device compared to warfarin therapy with three co-primary endpoints in 407 patients. In the first co-primary endpoint, the manufacturer reported a successful adverse event rate of 2.2%. The second co-primary endpoint did not meet pre-specified criteria for efficacy of all stroke, cardiovascular death, and systemic embolism at 18 months. The third co-primary endpoint met pre-specified criteria for occurrence of late ischemic stroke and systemic embolism at 18 months.

- **Key Expert Comments:** Experts commenting on this intervention generally agreed that data showed it would reduce stroke incidence in patients with AF. However, several experts noted that it would not completely eliminate the need for long-term anticoagulant therapy. Given the lack of compliance with preventive treatment, experts suggested that the device has the potential to reduce patient dependency on medications. Experts generally anticipated widespread adoption by both patients and clinicians. However, some experts noted insufficient information regarding long-term safety and efficacy. The initial cost of device implantation could be offset potentially if it prevents stroke and obviates or decreases the need for anticoagulation therapy, experts commented. Overall, experts opined that this intervention has potential to fulfill the unmet need of safe and efficacious treatments for stroke prevention in patients with AF, but they would like to see data on longer term outcomes.
- **Potential for High Impact:** Moderately high

Genetic Disorder: Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is an inherited disorder that causes accumulation of high levels of low-density lipoprotein (LDL) cholesterol (LDL-C) due to a defect on chromosome 19 that impairs the LDL receptor's ability to remove LDL from the bloodstream. According to the U.S. National Human Genome Research Institute, FH can cause premature onset of coronary artery disease, myocardial infarction, and cardiac-related death. FH is an autosomal dominant disorder, meaning a defect needs to be present on only one of two number 19 chromosomes for the person to be affected. Patients who have inherited only one defective LDL receptor gene are said to have heterozygous FH. In rare instances, the genetic defect is inherited from both parents, causing a

genetic condition known as homozygous (Ho) FH, which exhibits increased severity compared with heterozygous FH. According to the Familial Hypercholesterolemia Foundation, heterozygous FH occurs in approximately 1 of every 500 persons and HoFH occurs in approximately 1 of every 1 million persons in the United States. Experts commented on one intervention with potential high impact in treating FH.

Lomitapide (Juxtapid) for Treatment of Homozygous Familial Hypercholesterolemia

- **Key Facts:** Lomitapide is a microsomal triglyceride transfer protein inhibitor that is indicated as a daily oral therapy for treating HoFH. In December 2012, FDA approved lomitapide (Juxtapid™) for marketing. In the trial (n=29) that served as the basis for the approval, Cuchel et al. (2013) reported that lomitapide at a median dose of 40 mg per day reduced LDL-C concentrations by a mean of 50% at 26 weeks from baseline. By week 56, LDL-C concentrations were reduced by 44% (95% confidence interval [CI], -57% to -31%; $p<0.0001$). At week 78, LDL-C concentrations were reduced by 38% (-52% to -24%; $p<0.0001$). The most commonly reported adverse events were gastrointestinal symptoms. Four patients had aminotransaminase levels measured at more than five times the upper limit of normal; the increase resolved after dose reduction or temporary halt of lomitapide therapy. No patient permanently stopped lomitapide because of liver abnormalities. Retail prices for a 30-day lomitapide supply range from more than $26,000 for 5 mg tablets to more than $29,000 for 20 mg tablets (as of June 2014) with the use of a coupon. Representative, private, third-party payers that include lomitapide in their drug formularies typically have preauthorization and step-therapy policies in place that govern coverage of the drug. Some payers place quantity limits on the drug and require annual recertification and documentation of patients' positive clinical response from lomitapide before approving prescription renewals. With regard to diffusion, the company reports continued quarterly domestic growth with plans for further expansion in the international market.
- **Key Expert Comments:** Experts generally agreed that lomitapide has a moderate to high potential to fill the unmet need for effective treatment for HoFH, given that it may serve as a bridge between conventional lipid-lowering drugs, such as statins, and invasive treatments, such as apheresis, which is costly, labor-intensive, and may not be readily accessible to all patients with this rare condition. Experts agreed that lomitapide would likely be adopted widely by both patients and clinicians for the targeted population of patients with HoFH, but noted cost to be the major barrier to acceptance. Experts generally commented that this intervention could have a substantial impact in terms of cost, because of the long-term treatment requirements for patients with HoFH. Most experts noted that this intervention has the potential to reduce the need for invasive procedures if proved to be effective in the long term.
- **Potential for High Impact:** Moderately high

Heart Failure

HF adversely affects quality of life as well as life expectancy and can develop from any condition that overloads, damages, or reduces the heart muscle efficiency, impairing the ventricles' ability to fill with or eject blood. In 2009, one in nine death certificates mentioned HF and it was the underlying cause in 56,410 of these 274,601 deaths. Based on data from 2007 to 2010 from the National Health and Nutrition Examination Survey, 5.1 million people older than the age of 20 years in the United States have HF. Approximately 50% of people with HF die within 5 years of

diagnosis. HF prevalence has increased during the past 20 years, and the number of patients who progress to end-stage HF is expected to grow because of increased survival in patients with coronary artery disease, an increased population of aging patients, and significant advances in the control of other potentially lethal diseases. Projections suggest that the prevalence of HF will increase 25% from 2013 to 2030, and costs will increase 120%. The estimated cost of HF in the United States in 2013 was $32 billion. Because of the clear unmet need for effective therapies for HF and its underlying cause, many new drugs, biologics, and devices are under study for treating patients who have HF. Experts thought one intervention had potential high impact for treating HF.

Portable Freedom Driver for In-Home Support of the Total Artificial Heart

- **Key Facts:** The Freedom® Driver System, made by SynCardia Systems, Inc., of Tucson, AZ, is a wearable, pneumatic, portable driver under development to enable at-home support for the company's temporary Total Artificial Heart (TAH-t) in patients awaiting a heart transplant. FDA in October 2004 approved the TAH-t as a bridge to transplantation. It is indicated for use in cardiac transplant–eligible patients at risk of imminent death from nonreversible biventricular failure. The TAH-t is traditionally powered by a conventional pneumatic driver system, which is a large and cumbersome device that requires patients to remain hospitalized while awaiting a donor heart. A portable driver system that might allow patients to be discharged from the hospital while awaiting a suitable donor heart would address a significant unmet need for the relatively small number of people in this patient population. The battery-powered Freedom Driver System weighs 13.5 lb and is carried by the patient in a backpack or shoulder bag. As with conventional, large, hospital-based pneumatic driver systems, the Freedom driver is connected to the implantable TAH-t by a flexible pneumatic driveline that passes through the patient's skin in the left chest just below the ribs. The driver flashes a light or sounds an alarm when the system requires the user's attention. A clinical trial of the driver is ongoing. The company reported that as of October 2013, 86 TAH-t patients had been enrolled in the Freedom driver clinical study (including five patients under compassionate use). Of these 86 patients, 62 had been discharged home using the Freedom portable driver. In June 2014, the company reported that a 74-year-old patient had lived with a TAH-t powered by the Freedom Driver for more than a year and that the youngest patient ever provided with a Freedom Driver, a 16-year-old girl, was discharged home.
- **Key Expert Comments:** Although this intervention is expected to have a significant impact on quality of life for patients with a TAH-t and may reduce health care costs associated with lengthy hospital stays while awaiting a heart transplant, the patient population for which this device is intended is small, which tempers its overall potential impact on the health care system, experts thought. However, they also thought that shifting care from the inpatient to the outpatient setting would be a very important effect of this intervention, if approved for marketing. Several experts commented that a shift to home care could potentially reduce cost for patients awaiting heart transplantation. However, other expert thought that the cost of equipment and home nursing care would be similar to inpatient care.
- **Potential for High Impact:** Lower end of the high-impact-potential range

Valve and Structural Disorders

This section includes topics that purport to address unmet needs for certain disorders of heart valves.

Aortic valve stenosis: This condition affects primarily the elderly and obstructs normal blood flow through the aortic valve, the most likely of the heart's four valves to fail because of disease. Severe, untreated aortic valve stenosis can eventually lead to HF or sudden cardiac arrest. According to researchers, in the United States, about 29% of people aged 65 years or older and 37% of people aged 75 years or older have aortic sclerosis, a precursor condition to aortic stenosis characterized by mild thickening or calcification of the aortic valve without restricted leaflet motion. About 1% to 2% of the population is living with a bicuspid aortic valve, a congenital defect in which the aortic valve develops two instead of three normal valve leaflets. According to Novaro (2011), half of this population will develop aortic stenosis. Experts commented on one intervention with potential for high impact in treating aortic valve stenosis.

Transcatheter Aortic Valve Implantation (CoreValve) for Treatment of Severe Aortic Stenosis

- **Key Facts:** New, minimally invasive approaches are making the therapeutic benefit of aortic valve replacement an option for patients with severe aortic stenosis who are not candidates for open-heart valve surgery or who are at high risk of complications from open-heart surgery. Transcatheter aortic valve implantation (TAVI) with the CoreValve® System is a newly approved, minimally invasive therapeutic option for treating or delaying end-stage HF due to aortic stenosis in patients at high risk of complications from open surgical valve replacement. The CoreValve System features a porcine pericardial tissue valve mounted in a self-expanding, hourglass-shaped, nitinol-alloy mesh frame. The bioprosthetic valve is deployed using an 18-French diameter delivery catheter with a set of disposable catheter-loading components in a procedure that lasts up to 4 hours and requires, on average, a 3- to 5-day hospital stay. The approval covers the entire CoreValve platform, including the 23 mm CoreValve Evolut and the CoreValve 26, 29, and 31 mm valves. In May 2012, CMS released a national coverage determination stating that CMS "covers transcatheter aortic valve replacement (TAVR) under Coverage with Evidence Development (CED)" when the procedure is used for "the treatment of symptomatic aortic valve stenosis when furnished according to an FDA approved indication." The coverage determination further requires that numerous conditions are met, including credentials and experience of the facilities and surgeons who perform the procedure. CoreValve is the second transcatheter aortic valve FDA has approved. Sapien, by Edwards LifeSciences Corp., was the first; CoreValve has more size options than Sapien. A related note is that Edwards LifeSciences received FDA approval in June 2014 for its next-generation valve, Sapien XT, which has a smaller profile and a third, larger size option (29 mm).
- **Key Expert Comments:** Experts commenting on this intervention agreed that it would offer an important and effective new treatment modality for patients who have no other effective medical options and are not candidates for open surgery. However, one expert noted the availability of a similar transcatheter heart valve. Experts thought that this intervention would significantly improve patient health outcomes. However, one expert was concerned with the potential need for permanent pacemaker implantation. Experts generally agreed on a high potential for this intervention to disrupt health care infrastructure and patient management, citing the need for significant capital and operational support for centers not

equipped to perform TAVI. Overall, experts anticipated widespread patient and clinician adoption due to the willingness of both groups to accept a minimally invasive approach.

- **Potential for High Impact**: High

Mitral regurgitation (MR): MR is defined broadly as a backward flow of blood from the heart's left ventricle into the left atrium during contraction. MR can be divided into two major categories: primary, or organic MR, and secondary, or functional MR (FMR). FMR is associated with poor long-term survival, and its presence in patients with ischemic and dilated cardiomyopathy is an independent risk factor for cardiovascular morbidity and mortality. According to Mayo Clinic investigators, without treatment, severe MR can lead to congestive HF or potentially life-threatening cardiac arrhythmias. Significant MR occurs in an estimated 1% to 2% (about 4 million) of the U.S. population. More than 250,000 cases of significant MR are diagnosed each year in the United States and about 50,000 people undergo some type of surgery for the disease, according to one manufacturer in the field. Experts commented on one intervention with potential high impact in treating MR.

Transcatheter Mitral Valve Repair (MitraClip) for Treatment of Mitral Regurgitation

- **Key Facts:** Transcatheter mitral valve repair with the MitraClip® device (Abbott Laboratories, Abbott Park, IL) is intended to simulate the functional effects achieved by standard open-surgery repair for treating MR. In the standard procedure, a surgeon sutures together the edges of the two opposing mitral valve leaflets at the center of the valve opening, leaving two smaller openings on either side that close more completely than a single large opening. In a MitraClip procedure, the physician uses a transcatheter approach in which a two-armed, flexible metal clip covered in polyester fabric is used, rather than the sutures used during open surgery. In 2013, Pleger and collaborators reported 1-year outcomes from 59 patients with severe, symptomatic MR and reduced ejection fraction who received MitraClip. Procedural efficacy was measured by the reduction in MR and improvement in New York Heart Association (NYHA) functional classification. Investigators reported that device implantation was associated with reduced MR and improved NYHA functional class, translating into improved 6-minute walk test distance. Followup echocardiography suggested a reversal in heart enlargement, with reduced left atrial volume and left ventricular end-systolic diameter and increased left ventricular ejection fraction (LVEF). These results were consistent with outcomes of a subgroup of 25 patients with severely reduced LVEF (23±2%), suggesting that sicker patients also reaped a benefit from MitraClip. Investigators reported 30-day mortality of 2.9%. Also in 2013, Grasso and co-authors reported outcomes from 117 patients in the GRASP Registry. These investigators reported acute procedural success in all patients and no procedure-related mortality.

  Outside the United States, the manufacturer issued a product recall in 2011 and a safety advisory in early 2013. Both issues were related to potential problems with the MitraClip delivery system that could malfunction and require emergency open-heart surgery to correct.

  MitraClip received the Conformité Européene (CE) mark for marketing in Europe in 2008 for use as a nonsurgical option in patients with severe MR. In October 2013, FDA granted marketing approval for the MitraClip delivery system for treating significant symptomatic degenerative MR. In the trial that served as the basis for the approval, Lim and co-workers (2013) reported results of a retrospective study of 127 patients with degenerative MR at prohibitive surgical risk. After FDA approval, Abbott requested a new technology

add-on payment from CMS. CMS denied the request, and Abbott reportedly stated intentions to make the request again, which if granted, would not take effect before October 2014 at the earliest. CMS initiated a national coverage analysis (NCA) for transcatheter mitral valve procedures in November 2013, and in May 2014, issued a Proposed Decision Memo stating that it proposes to cover transcatheter mitral valve procedures under coverage with evidence development when certain criteria are met. The NCA is expected to be completed by August 16, 2014.

Hospitals reporting device costs to ECRI Institute's PriceGuide database reported a cost range of $25,000 to $30,000 for the valve kit (as of June 2014).

- **Key Expert Comments:** Experts commenting on this technology generally agreed this procedure addresses a considerable unmet need and has the potential to improve patient health. However, most experts opined that more data concerning safety and long-term outcomes are needed, citing the potential for adverse events and the technically difficult nature of the procedure. Experts were split on whether this technology would disrupt health care delivery. Some experts believe it would not because the infrastructure is already in place, while other experts believe that the increase in case volume might cause a large disruption to health care delivery. The majority of experts believe use of the MitraClip will increase health care costs, but were not sure if those costs could be offset by a reduced need for standard therapy for this population. They said longer-term data are needed to determine this. Overall, experts opined that the benefits of this intervention outweigh the risks and that long-term data would determine its full potential.
- **Potential for High Impact:** Moderately high

Arrhythmia Intervention

Subcutaneous Implantable Cardioverter-Defibrillator (S-ICD) for Treatment of Life-Threatening Ventricular Tachyarrhythmias

Unmet need: Implantable cardioverter-defibrillators (ICDs) are an established therapy to prevent sudden cardiac arrest from ventricular arrhythmias. Conventional ICDs have a transvenous lead that is placed in the heart for cardiac sensing and defibrillation.[1] However, this transvenous lead can cause serious complications during and after implantation including cardiac tamponade, pneumothorax, and hemothorax (during lead implantation) and lead failure (after implantation).[1] Lead failure can generate unnecessary shocks or fail to provide necessary shocks, and removing faulty leads is often associated with significant morbidity and mortality. Lead problems have occurred in up to an estimated 40% of cases for some ICD models. This has prompted development of an ICD system that replaces conventional transvenous leads with a single, subcutaneous lead in the chest.[1-3]

Intervention: The Subcutaneous Implantable Cardioverter-Defibrillator (S-ICD®) System is indicated "to provide defibrillation therapy for the treatment of life-threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia that is reliably terminated with anti-tachycardia pacing" (i.e., the device is approved only for patients who do not require a pacemaker or pacing therapy).[4,5] The S-ICD System components consist of the SQ-RX® pulse generator, the Q-Trak® subcutaneous electrode, the Q-Guide™ electrode insertion tool, and the Q-Tech™ programming system.[6] The battery-powered, computer-controlled pulse generator is intended to detect cardiac activity and provide defibrillation energy to the heart through the single subcutaneous electrode; the manufacturer states that the battery lasts 5.1 years.[6,7] The external programmer is designed to allow clinicians to set parameters for the pulse generator and retrieve data.[6]

According to the manufacturer, a physician typically implants the S-ICD during an outpatient procedure using anatomic landmarks rather than fluoroscopic imaging guidance to position the device.[7-9] The implantation procedure can be performed with the patient under general or local anesthesia.[10] To implant the device, a physician creates a pouch for the pulse generator beneath the skin under the left arm using an incision along the rib cage around the fifth and sixth intercostal spaces at the mid-axillary line.[7] Two small incisions to the left of the sternum are used to thread the subcutaneous electrode under the skin and connect it to the pulse generator.[7] Before closing the incisions, the physician tests and adjusts the system using the external programmer.[7,8]

Clinical trials: In 2014, Lambiase and colleagues reported interim results from the EFFORTLESS prospective, postmarket observational study that suggested device implantation with the S-ICD had low complication rates. Among the 456 treated patients, investigators reported complication-free rates of 97% and 94% at 30 and 360 days, respectively. At 360 days, the inappropriate shock rate was 7%, primarily attributed to over-sensing of cardiac episodes.[11]

In February 2013, Jarman and colleagues reported on the early phase clinical experience using the S-ICD in the United Kingdom.[12] Investigators surveyed all UK hospitals implanting the S-ICD, of which 76% (19 of 25) of hospitals responded with data on 111 patients. Patients had a median age of 33 years (range 10–87 years). Underlying pathologies treated with the S-ICD included the following: primary electrical disease, 43%; hypertrophic cardiomyopathy, 20%; ischemic cardiomyopathy, 14%; congenital heart disease, 12%; idiopathic dilated cardiomyopathy, 5%; and other cardiomyopathies, 6%.[12] Overall, 17% of patients (19 of 111) required 20 repeat operations related to S-ICD placement, including 9% of patients (10 of 111) in whom the device was permanently removed.

During the study period, S-ICDs delivered 24 appropriate shocks, including 10 shocks for ventricular fibrillation, in 12% of patients (13 of 111). One patient died from a cardiac arrhythmia, but investigators found no instances of the device failing to detect or treat (defibrillate) ventricular arrhythmias above the programmed detection rate. Devices delivered 51 inappropriate shocks in 15% of patients (17 of 111). Among inappropriate shocks, 80% (41 of 51) were due to T-wave oversensing. Patients who received inappropriate shocks due to T-wave oversensing were significantly younger than patients who did not (24±10 vs. 37±19 years; p=0.02).[12]

Manufacturer and regulatory status: Boston Scientific Corp. (Natick, MA) makes the S-ICD, having acquired the device's developer, Cameron Health, in 2012.[13] In the United States, the U.S. Food and Drug Administration (FDA) approved the S-ICD in September 2012.[5] As part of the approval, FDA required a 5-year, 1,600-patient postmarket study to assess the device's long-term safety and performance and to assess differences in effectiveness between sexes.[5] The device received the Conformité Européene (CE) mark in 2009 for distribution in Europe.[13]

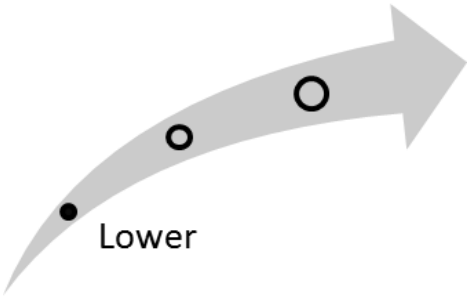
Diffusion: Boston Scientific planned a phased launch of the system in the United States to ensure that clinicians are trained to use the system in a safe and effective way.[4] In April 2013, a report in the periodical *Medical Device and Diagnostic Industry* stated that demand was outstripping supply, and a company spokesperson was quoted as saying the supply would remain limited until the next generation of the device was launched in late 2013.[14] The American Medical Association Current Procedural Terminology has established category III codes for the S-ICD to enable tracking of its use.[15]

Per-patient cost for the device and procedure is about $35,000.[16] The device's cost is reported to be similar to that of conventional transvenous-lead ICDs; however, costs of the procedure may be less than conventional ICD implantation because it can be performed in an outpatient setting in a shorter time frame, with no need for fluoroscopy or an electrophysiology laboratory.[9] Use of the device may also reduce ICD costs by avoiding complications associated with conventional ICDs. The U.S. Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) on ICDs does not mention the S-ICD specifically, but ICDs that FDA has approved are covered as medically necessary when a beneficiary meets certain eligibility criteria.[17,18] In private, third-party payer coverage policies addressing ICDs (generally updated or revised after FDA approval of the S-ICD), several major payers that publish their coverage policies online consider the S-ICD to be investigational or experimental and deny coverage at this time, noting a desire for safety and efficacy data that are equivalent to transvenous ICDs. Among the payers that provide coverage consistent with the Medicare NCD at this time for the S-ICD are Blue Cross/Blue Shield Massachusetts[19] and United Healthcare.[20]

Clinical Pathway at Point of This Intervention

According to the American College of Cardiology (ACC) and the American Heart Association (AHA), prophylactic ICDs are the preferred treatment for patients with ventricular fibrillation who are at risk of sudden cardiac arrest. For patients who do not meet criteria for an ICD, beta blockers are considered first-line therapy, and radiofrequency (RF) ablation might be indicated. For patients with ventricular fibrillation refractory to ICD, drug therapy and RF catheter ablation or antiarrhythmic surgery might be warranted.[21] The S-ICD system competes directly with standard ICD systems that require a transvenous electrode in the heart. Clinicians might prefer the S-ICD System to other ICD systems because it offers the potential to reduce procedure-related complications and lead-related adverse events and does not require imaging during placement.

Figure 1. Overall high-impact potential: Subcutaneous Implantable Cardioverter-Defibrillator (S-ICD) for treatment of life-threatening ventricular tachyarrhythmias



Overall, experts commenting on this topic thought that S-ICDs have potential to improve patient health outcomes by reducing complications associated with lead-based ICDs that carry a high risk of morbidity and some mortality. Experts noted that this device might supply fewer inappropriate shocks than conventional ICDs. Because the implantation procedure requires fewer resources and can be performed in an outpatient setting, this intervention could shift care delivery and shorten hospital stays. However, some experts suggested that this device's limited capabilities, compared with other ICDs, might temper its diffusion and impact on patient health outcomes. Based on this input, our overall assessment is that this intervention is in the lower end of the high-impact-potential range.

Results and Discussion of Comments

Five experts, with clinical, research, health systems, and health administration backgrounds, offered perspectives on this intervention.[22-26] One of these experts declared a potential conflict of interest (COI) because the expert is an electrophysiologist who acts as a consultant to Boston Scientific and Medtronic, Inc., another manufacturer of cardiac devices.[25] This potential COI is balanced by the perspectives of other experts who reported having no COIs. We have organized the following discussion of expert comments according to the parameters on which they commented.

Unmet need and health outcomes: Experts generally agreed that current treatment methods are associated with safety concerns and that safe and effective devices are needed. However, some experts were unsure if patients who experience lead complications with conventional ICDs would be good candidates for this intervention. One expert representing a health systems perspective opined, "Current treatment methods to treat cardiomyopathy (i.e., conventional ICDs) are full of adverse events due to the invasiveness of the lead implantation. This results in significant morbidity and mortality rates. Therefore there is moderate importance for a new treatment method with less potential for adverse events."[26]

Most experts commenting on this intervention agreed that it could improve patient health outcomes. They cited a significant reduction in lead failures and other adverse events associated with standard ICDs. However, several experts expressed concerns over inappropriate shock rates observed in clinical trials.

Acceptance and adoption: Both patients and clinicians would likely adopt this device if it shows good efficacy relative to existing ICDs, the experts agreed. However, a few experts suggested that longer-term data will be necessary before clinicians fully embrace the technology and thought that diffusion might be constrained by the device's limited pacing capabilities. Experts noted that patients would be more willing to accept treatment with this intervention due to the less-invasive nature of the procedure.

Health care delivery infrastructure and patient management: Because ICD placements are common, this intervention is unlikely to significantly disrupt care models or operational processes, with a few exceptions, experts noted. Experts suggested that the device can be implanted in an outpatient setting, which would shift care from the inpatient to outpatient setting. One expert representing a

research perspective opined, "The same specialist physicians (electrophysiologists) who implant conventional ICDs would likely implant subcutaneous ICDs, and do so in the same healthcare facilities."[22] However, they noted that some initial S-ICD-specific training may be required.

Health disparities: Experts generally agreed that the S-ICD has minimal potential to affect health disparities among patients who might be candidates for ICD therapy. Although the S-ICD's cost is similar to that of other ICD systems, experts thought that by avoiding lead complications and shifting the setting from inpatient to outpatient surgery, this intervention has the potential to reduce some financial burden.

Atrial fibrillation–Associated Stroke Intervention

Percutaneous Left Atrial Appendage Occlusion (Watchman) for Prevention of Atrial Fibrillation–Associated Stroke

Unmet need: Patients with atrial fibrillation (AF) are at high risk of developing stroke due to thrombi forming in the left atrial appendage (LAA).[27-30] Anticoagulant therapy is used in an attempt to prevent stroke in patients with AF, but an estimated 14% to 44% of patients with AF have bleeding risks that preclude them from taking anticoagulants.[27,31] Additionally, the need for frequent monitoring, dosage adjustments, and dietary restrictions make standard anticoagulant therapy with warfarin a less-than-optimal therapy with discontinuation rates estimated to be about 38% per year.[31] Although newly approved anticoagulant alternatives to warfarin, (e.g., apixaban, dabigatran, rivaroxaban) eliminate the need for routine monitoring and dietary restrictions, these therapies have other drawbacks, including nonhemorrhagic side effects, potential for drug-drug interactions, and no antidote in the event of uncontrolled bleeding.[32,33]

Intervention: The Watchman device is a permanent implant that is placed in the LAA to prevent strokes in patients with AF. Stroke prevention is accomplished by occluding the LAA opening to prevent clots that otherwise might have formed in the LAA from entering circulatory system.[34] The Watchman LAA Closure Technology consists of three components: a delivery catheter and transseptal access sheath, which is used to access the LAA and serves as a conduit for the delivery catheter; a self-expanding nitinol frame with a permeable polyester fabric that is preloaded within the delivery catheter; and fixation barbs on the frame that allow the device to be secured in the LAA. Once the device is expanded, the fabric covers the atrium-facing surface of the device. The system is available in five sizes (i.e., 21, 24, 27, 30, and 33 mm).[34,35]

Implantation is performed during a percutaneous catheterization procedure, using a standard transseptal technique and fluoroscopic guidance. Before catheterization, clinicians perform a transesophageal echocardiogram to assess the LAA anatomy to determine the appropriate device size for the patient. According to the manufacturer, the implantation procedure lasts about 1 hour and can be done under local or general anesthesia. Patients can typically leave the hospital 24 hours after the procedure, but require anticoagulant therapy.[36] A minimum of 45 days of warfarin therapy after device implantation is required for patients in whom warfarin is not contraindicated. For patients who have contraindications to warfarin anticoagulation, the manufacturer recommends treatment with 75 mg clopidogrel and an adult aspirin dose daily for up to 6 months, followed by a once-daily adult aspirin dose indefinitely.[35]

Clinical trials: In March 2013, the manufacturer reported results from a confirmatory study requested by FDA. The PREVAIL trial (n=407) evaluated safety and efficacy of the device compared with warfarin therapy for three co-primary endpoints. The manufacturer reported an adverse-event rate of 2.2%, with an upper bound on the confidence interval (CI) of 2.62% versus a prespecified threshold of 2.67%. The second endpoint did not meet pre-specified criteria for efficacy of all stroke, cardiovascular death, and systemic embolism at 18 months. The third endpoint met pre-specified criteria for occurrence of late ischemic stroke and systemic embolism at 18 months. The observed adverse-event rate in the device group was 0.0253 per 100 patient years (CI upper bound 0.0268, versus prespecified 0.0275).[37] All patients are enrolled in a 5-year long-term followup analysis.

In February 2013, Reddy and colleagues reported results of a 2.3-year followup of primary efficacy from the PROTECT AF trial. Investigators observed primary efficacy event rates of 3.0% and 4.3% in the device and control groups, respectively. Primary safety events occurred in 5.5% per year in the device group compared with 3.6% per year in the control group.[38]

Additional adverse events observed in patients implanted with the Watchman device in the PROTECT AF trial include gastrointestinal bleeding (2.2.%), ischemic stroke likely caused by air embolism from the transseptal sheath (1.1%), device embolization (0.6%), bleeding requiring transfusion (0.4%), cranial bleed (0.4%), arrhythmias (0.2%), bruising (0.2%), esophageal tear from the probe (0.2%), and hemorrhagic stroke (0.2%).[39]

Manufacturer and regulatory status: The Watchman device was developed by Atritech, Inc. (Minneapolis, MN),[40] which was acquired by Boston Scientific in 2011.[41] The device is limited to investigational use in the United States.[40] Atritech filed a premarket approval application (PMA) with FDA in 2008.[42] In 2010, FDA "requested that a confirmatory study be conducted to further substantiate the safety and effectiveness of the Watchman LAA Closure Technology in patients with AF at risk of stroke and eligible for anticoagulation therapy."[43]

Based on the results of the PREVAIL trial and earlier trials, Boston Scientific submitted an amended PMA to FDA. In December 2013, the Circulatory System Devices Panel of FDA's Medical Devices Advisory Committee voted to recommend that FDA grant Boston Scientific marketing approval for its Watchman device to reduce the risk of embolic stroke in patients with AF.[44] The panel voted 13-1 in favor of approval for each of three criteria: (1) that Watchman's benefits outweigh its risks, (2) that reasonable assurance of Watchman's safety exists, and (3) that reasonable assurance of Watchman's efficacy exists. Boston Scientific anticipated FDA's decision on marketing approval for the Watchman by the end of June 2014.[44] June 17, 2014, the company announced at an investor conference that FDA had just rendered a decision requiring the device to go before a third advisory panel for consideration before a final decision could be made. [45] The company does not expect an FDA approval decision until the first half of 2015.[46]

The device was CE marked, allowing marketing in Europe, in 2005 and was commercialized outside the United States in 2009. In 2012, the European Union expanded indications for Watchman to include use of the device in patients in whom warfarin therapy is contraindicated.[35,47]

Boston Scientific is also developing a next-generation Watchman device that purportedly reduces the potential for damage leading to pericardial effusion.[48]

Diffusion: If approved for marketing, the device will likely compete with the anticoagulants warfarin, apixaban, dabigatran, rivaroxaban, heparin, and aspirin. The Watchman device may also compete with surgical exclusion of the LAA or percutaneous LAA occlusion performed with the FDA-cleared Lariat® suture delivery device.[49,50] Additionally, several investigational percutaneous LAA occlusion devices may compete with the Watchman device if approved in the United States. These devices include the Coherex Wavecrest™ LAA occluder system[51] and the Amplatzer™ cardiac plug.[52]

Costs for LAA occlusion with the Watchman device have not been established in the United States. In the United Kingdom, total costs for the Watchman implantation procedure and device are estimated at about £11,400 with the device costing approximately £5,300, and the implantation procedure costing approximately £6,000.[53] At April 2014 currency exchange rates, those estimated total costs would be approximately $19,052 including $8,824 for the device and $9,989 for the implantation procedure.[54]

At this time, CMS does not have a national coverage determination for LAA occlusion with the Watchman device or other LAA occlusion devices. Thus, coverage is left to the discretion of local Medicare carriers.

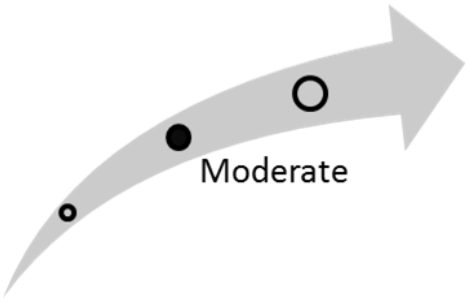
ECRI Institute searches of a group of representative, private third-party payers that publish their coverage policies online found a number of payers that consider percutaneous or transcatheter LAA occlusion with the Watchman and/or other similar devices to be investigational or experimental and therefore deny coverage for the procedure. Payers that deny coverage include Aetna,[55] Anthem,[56] Blue Cross Blue Shield (BCBS) of Alabama,[57] BCBS of Massachusetts,[58] BCBS and BlueCare

Network of Michigan,[59] BCBS of North Carolina,[60] BCBS of Tennessee,[61] CIGNA,[62] Empire BCBS,[63] HealthNet,[64] Regence,[65] and UnitedHealthcare.[66]

Clinical Pathway at Point of This Intervention

A serious complication of AF is ischemic stroke.[27,28] Risks for ischemic stroke after all standard stroke risk factors are accounted for are four- to fivefold greater in patients with AF than in other individuals.[28] Stroke risk is high in AF because thrombi form in the atria or, more commonly, in the left atrial appendage.[29,30] A stroke results when a part of a thrombus breaks off into the systemic circulation and travels to the brain, blocking blood flow to an area there. Thromboembolism is prevented through antithrombotic pharmacologic therapy. Guidelines recommend that the choice of antithrombotic drug be based on the absolute stroke and bleeding risks and the patient's relative risks and benefits.[27] Antithrombotic agents include vitamin K antagonists, aspirin, low-molecular-weight heparin, and oral anticoagulants apixaban, dabigatran, and rivaroxaban.[27,33,67] The Watchman may potentially be positioned as an alternative to anticoagulant therapy for stroke prevention in patients with AF.[34]

Figure 2. Overall high-impact potential: percutaneous left atrial appendage occlusion (Watchman) for prevention of atrial fibrillation–associated stroke



Overall, experts commenting on this topic agreed that it would reduce stroke incidence in patients with AF. However, several experts noted that it would not eliminate the need for long-term anticoagulant therapy. Experts suggested that the device has the potential to reduce patient dependency on these anticoagulant pharmacotherapies. Experts cited long-term safety and efficacy to be the most significant barrier to otherwise anticipated widespread patient and clinician adoption. Experts generally agreed that initial costs associated with this intervention could be alleviated if proved to improve patient medication compliance and reduce incidence of stroke. Based on this input, our overall assessment is that this intervention is in the moderate high-impact-potential range.

Results and Discussion of Comments

Six experts, with clinical, research, health systems, and health administration backgrounds, offered perspectives on this intervention.[68-73] We have organized the following discussion of expert comments according to the parameters on which they commented.

Unmet need and health outcomes: Overall, experts commenting on this intervention agreed that treatment options are limited to prevent and reduce stroke incidence in patients with AF. The device has the potential to improve patient health outcomes, experts agreed. Several cited the potential of the device to reduce dependency on anticoagulant therapy.[70,72,73] However, they also noted that it would not completely eliminate the need for long-term anticoagulant therapy. One expert with a health systems perspective opined, "The intervention is really more of a supplemental treatment option as it does not eliminate the need for warfarin therapy (current standard of care) but rather acts as a fail-safe should clots persist despite the treatment option."[73]

Acceptance and adoption: Experts generally anticipated widespread adoption by both patients and clinicians. However, some noted insufficient information regarding long-term safety and efficacy. One clinical expert anticipated wide clinical acceptance but also listed cost and eligibility as potential barriers.[68] An expert representing a research perspective commented, "Long-term follow-up data that support the safety and efficacy of Watchman is still insufficient. Non-inferiority design and the composite outcome measures used in the trials did not provide firm evidence to show Watchman is better than current standard of care."[72] Experts anticipated that patients would be more willing to accept a less-invasive procedure, but listed safety, efficacy, and cost as potential barriers.

Health care delivery infrastructure and patient management: Most experts commenting on this intervention did not anticipate a major disruption to health care deliver infrastructure. They generally agreed that device implantation could be performed in existing infrastructures, but that some training would be required. One expert with a health systems perspective commented, "The Watchman device will need specific training and experience for successful and safe implantation. Such catheter-guided procedures may impact cath lab utilization."[69] Another expert with a research perspective noted a potential increase in case volume.[72]

Health disparities: Experts did not think this technology would affect health disparities. However, several experts thought cost would be a factor for patients without health insurance. One expert representing a clinical perspective commented, "This will be an expensive device therapy. Uninsured patients and those with less-generous health plans may find these high-cost device therapies out of reach. This may in fact worsen the health disparities in the overall population."[68]

Genetic Disorder Intervention

Lomitapide (Juxtapid) for Treatment of Homozygous Familial Hypercholesterolemia

Unmet need: Homozygous familial hypercholesterolemia (HoFH) occurs in 1 of every 1 million people in the United States.[74] Despite the availability of lipid-lowering pharmacotherapies, many patients with HoFH do not achieve target lipid levels and remain at increased risk of having early coronary events and sudden death.[75] Nonpharmacologic interventions, such as apheresis and liver transplantation, are costly, invasive, and not widely available. One other drug, mipomersen sodium (Kynamro®), is available for patients with HoFH as a weekly subcutaneous injection as an adjunct to lipid-lowering drugs and diet to reduce low-density lipoprotein cholesterol (LDL-C), apolipoprotein-B (apo-B), total cholesterol, and non–high-density lipoprotein cholesterol (non–HDL-C).[76,77] Effective oral, self-administered therapy is needed; lomitapide (Juxtapid™) was recently approved to address this need.

Intervention: Lomitapide is a microsomal triglyceride transfer protein (MTP) inhibitor that is indicated as a daily oral therapy for treating HoFH.[78] MTP is a lipid transfer protein that assists in assembling two lipoproteins: chylomicrons and very-low-density lipoproteins (VLDLs). MTP assists in the assembly by transferring triglycerides onto apo-B, an essential component of chylomicrons and VLDL.[79,80] In essence, MTP binds and shuttles individual lipid molecules from the site of their synthesis (in either the intestine or the liver) to an emerging apo-B molecule, which then forms a chylomicron in the intestine or VLDL in the liver.[79,80] Lomitapide prescribing information advises to begin treatment at 5 mg once daily and to escalate dosage gradually based on acceptable safety and tolerability to 10 mg daily after at least 2 weeks; dosage may be increased at a minimum of 4-week intervals, to 20 mg, 40 mg, and up to the maximum recommended dose of 60 mg daily.[81]

The manufacturer claims that "if insufficient lipid is transferred to the apo-B molecule, the emerging apo-B is destroyed and lipoprotein secretion is inhibited;" therefore, "inhibition of MTP activity prevents both hepatic VLDL and intestinal chylomicron secretion, and consequently lowers plasma lipids."[79] Lomitapide is self-administered orally, once daily, without food.[82]

Clinical trials: FDA approval of lomitapide was based on review of a trial that evaluated the drug in 29 patients with HoFH.[83,84] The median dose was 40 mg per day. Lomitapide reduced LDL-C concentrations by a mean of 50% at 26 weeks from baseline. By week 56, LDL-C concentrations remained reduced by 44% (95% confidence interval [CI], -57 to -31; $p<0.0001$). At week 78, LDL-C concentrations were reduced by 38% (-52 to -24; $p<0.0001$). In the trial, the most commonly reported adverse events were gastrointestinal symptoms. Four patients had aminotransaminase levels measured at more than five times the upper limit of normal; the increase in aminotransaminase levels resolved after dose reduction or temporary halt of lomitapide therapy, but remains a concern for patients on therapy. During the trial, researchers reported that no patient permanently stopped lomitapide because of liver abnormalities.[83,84]

In November 2013, the manufacturer reported results from a phase III extension study of 19 patients with HoFH. At week 126, mean LDL-C concentrations were reduced by 45.5% (356±127 mg/dL vs. 189±120 mg/dL; $p<0.001$).[85]

Manufacturer and regulatory status: Lomitapide is manufactured by Aegerion Pharmaceuticals, Inc. (Cambridge, MA).[78] In December 2012, FDA approved lomitapide capsules as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce LDL-C, total cholesterol, apo-B, and non–HDL-C in patients with HoFH.[84] Lomitapide has boxed warnings on its product label advising of a risk of severe liver toxicity (as does the injectable drug for HoFH, mipomersen sodium).[76,81,86] Likewise, it (and mipomersen) is available only in concert with a Risk Evaluation and Mitigation Strategy (REMS) program.[76,81,86]

The REMS program requires the manufacturer to certify prescribing physicians and dispensing pharmacies to use the drug and to document safe-use conditions, including a prescription authorization form for each new prescription.[76] For lomitapide, the program also requires that liver function tests be performed in patients before administration and at intervals during and after administration.

The company must also conduct three postmarketing studies for lomitapide: an animal study to evaluate potential drug toxicity in pediatric patients; a long-term patient registry to determine long-term safety; and an enhanced pharmacovigilance program to monitor reports of malignancy, teratogenicity, and hepatic abnormalities.[84]

In May 2013, Aegerion announced that the European Committee for Medicinal Products for Human Use had adopted a positive opinion with a unanimous vote recommending a marketing authorization in the European Union for lomitapide (to be marketed as Lojuxta™) capsules for a similar indication.[87] In August 2013, Aegerion announced that it had received approval from the European Commission.[88]

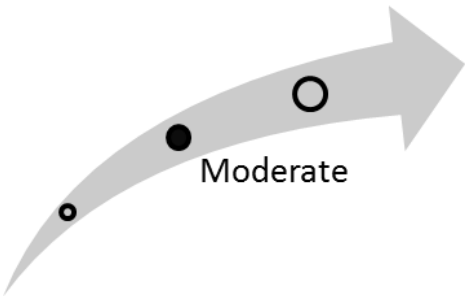
Diffusion: In May 2014, the company reported a 24% quarterly growth in net product sales in the United States. The company announced that it had initiated a phase III clinical trial in Japan and expected continued market share growth in the United States and Brazil.[89]

CMS does not have a national coverage determination for lomitapide, so coverage is at the discretion of local Medicare D prescription drug plans. Representative, private, third-party payers that include lomitapide in their drug formularies have precertification and step-therapy policies in place that govern coverage of the drug.[90-96] Some of these payers place quantity limits on the drug and require annual recertification and documentation of patients' positive clinical response from lomitapide before allowing prescription renewals.[90,95] According to a U.S.-based, online aggregator of prescription-drug prices, a 30-day supply of lomitapide ranges from $26,374 for 5 mg tablets to $29,638 for 20 mg tablets with the use of a coupon (as of June 2014).[97] Thus, the annual per-patient retail cost is more than $315,000.

Clinical Pathway at Point of This Intervention

According to the National Human Genome Research Institute, first-line treatment for patients with HoFH includes lifestyle changes (e.g., diet, exercise) and drug therapy with cholesterol-lowering medications (e.g., statins, bile acid sequestrants, ezetimibe, niacin, gemfibrozil, fenofibrate).[98] For these patients, these therapies are often insufficient, and more aggressive treatment is needed, including periodic apheresis or, possibly, a liver transplant.[98] The FDA-approved indication for lomitapide is as an adjunct to a low-fat diet and other lipid-lowering treatments to reduce LDL-C, total cholesterol, apo-B, and non–HDL-C in patients with HoFH.[84]

Figure 3. Overall high-impact potential: lomitapide (Juxtapid) for treatment of homozygous familial hypercholesterolemia



Overall, experts agreed that for the relatively small number of patients with HoFH, lomitapide has moderate to strong potential to fill the treatment gap between conventional lipid-lowering drugs (e.g., statins) and invasive, resource-intensive treatments such as apheresis and, in rare instances, liver transplantation. Experts agreed that lomitapide would likely be adopted widely by both patients and clinicians for the targeted population of patients with HoFH but noted cost to be the major barrier to acceptance. Most experts commented that this intervention has the potential to reduce the need for invasive procedures if proved to be effective in the long term. Based on this input, our overall assessment is that this intervention is in the moderate high-impact-potential range.

Results and Discussion of Comments

Seven experts, with clinical, research, health systems, and health administration backgrounds, offered perspectives on this technology.[99-105] We have organized the following discussion of expert comments according to the parameters on which experts commented.

Unmet need and health outcomes: For the small population of patients with HoFH, no effective oral pharmacologic therapy has been available to bridge the gap between conventional lipid-lowering drugs (e.g., statins) and the need for apheresis or, in rare instances, liver transplantation, the experts noted. Experts generally agreed that lomitapide holds potential to improve patient health, citing the potential of the drug to significantly reduce LDL. However, some experts cited the potential for adverse events and agreed on the need for more long-term clinical data. One expert representing a clinical perspective commented, "Drug lowers LDL cholesterol by about 50%. However, there is significant side effect of hepatic steatosis in nearly every treated patient. This is a major limiting factor."[99]

Acceptance and adoption: Experts generally agreed on the potential for this intervention to be widely adopted by patients and clinicians. As an adjunct to a low-fat diet and other lipid-lowering treatments to reduce LDL-C, total cholesterol, apo-B, and non–HDL-C, clinicians are likely to prescribe this drug to patients with HoFH, according to the experts. Most experts noted the ease of self-administering an oral medication to be attractive for both patients and clinicians. Several experts listed cost as a major barrier for patient and clinician acceptance, but noted that it would more likely affect patients. A health systems expert opined that the high drug cost could be potentially equal to the cost of treating progressive HoFH, "Expensive pharma medications are widespread in the healthcare system. The high cost of this medication is comparable to the costly surgical interventions a patient can likely expect with uncontrolled disease progression."[104]

Health care delivery infrastructure and patient management: Overall, most experts who provided comments thought that using lomitapide would create little to no disruption to the health care delivery infrastructure or disease management practices for this patient population.

Lomitapide has the potential to reduce the need for apheresis or liver transplantation, noted one expert representing research perspective.[102] Another research expert commented that liver function testing of patients for the duration of their lomitapide treatment would affect patient management.[103] One health systems expert thought the therapy would not present major disruptions to patient care, "Preauthorizations are very common for cardiac medications given the expense and intensity of patient education that go hand in hand, so even the REMS criteria will not present a significant disruption."[104]

Health disparities: Several experts cited cost as a major barrier for patients without insurance coverage and even for patients with insurance who could have significant co-payments. One expert representing a research perspective opined, "The cost of this treatment is exceptionally high, which may lead to a health disparity between economic classes. It will almost be a certainty that without

insurance, patients will not be able to receive this treatment.... This will create a noticeable divide between patients with insurance and those without."[100]

Heart Failure Intervention

Portable Freedom Driver for In-Home Support of the Total Artificial Heart

Unmet need: Historically, artificial heart technology has involved using large, hospital-based pneumatic driver systems that require patients to be hospitalized and tethered to a driver console. The standard 400-pound console powers the implantable components while patients await availability of a suitable donor heart.[106,107] An option that would allow these patients to leave the hospital and receive artificial-heart support at home while awaiting a donor heart has the potential to lower treatment costs and improve quality of life.[108]

Intervention: The temporary Total Artificial Heart (TAH-t) is a biventricular, implantable device that functions in place of the two ventricles and four valves of a failing heart by pumping blood to both the pulmonary and systemic circulations via a conventional external pneumatic driver system.[109,110] The driver system is large and cumbersome and requires patients to remain hospitalized while awaiting a donor heart.[108] To enable patients to leave the hospital and await a suitable donor heart at home, the TAH-t manufacturer has developed and is testing the 13.5 lb Freedom® Driver System. The portable driver is a wearable pneumatic device that powers the existing SynCardia TAH-t, which is indicated for use as a bridge to heart transplantation.[106]

To implant the TAH-t, a surgeon first removes the left and right ventricles and the four native valves of the failing heart. The surgeon then replaces the excised heart chambers and valves with the TAH-t, which replicates their function, in a procedure similar to heart transplantation.[111]

As with conventional hospital-based pneumatic driver systems, the Freedom Driver connects to the implantable TAH-t by a flexible pneumatic driveline that enters the body through the skin in the left chest just below the ribs. The driver sounds an alarm and/or flashes a light when it requires the user's attention. Two onboard batteries, which can be recharged using either a standard electrical outlet or automobile charger, power the portable Freedom Driver. The pneumatic driver is designed for patients to wear in a backpack or shoulder bag.[108]

Clinical trials: Literature searches have not identified any completed, published clinical trials using the Freedom Driver System, although the company has reported some preliminary results for 41 patients in the Freedom Driver IDE (FDA investigational device exemption) trial. The clinical experience of one individual patient has been published as a case summary.[112]

The FDA-approved IDE trial, the SynCardia Freedom Driver System Study, is permitted to enroll 60 patients across 40 sites. A minimum of 30 patients must be discharged home using the portable Freedom Driver, The study was originally scheduled for completion in October 2013.[107] The company reported that as of October 2013, 86 TAH-t patients had been enrolled in the Freedom Driver clinical study (including five patients under compassionate use).[108] Of these 86 patients, 62 had been discharged home using the Freedom portable driver. In June 2014, the company reported in press releases that a 74-year-old patient had lived for more than a year with a TAH-t powered by the Freedom Driver.[113] In May 2014, the company reported that the youngest patient to date, a 16-year-old female with a TAH-t implanted one year ago, was discharged to home care in May 2014 using a Freedom Driver.[114] Earlier press releases have been issued on several other cases,[112,115-118] one of whom had been supported for 949 days as of April 1, 2014.[119]

Manufacturer and regulatory status: SynCardia Systems, Inc. (Tucson, AZ), makes the TAH-t and Freedom Driver. In October 2004, FDA approved the TAH-t as a bridge to transplant.[120] As noted above, the portable Freedom Driver is under evaluation in an FDA-approved IDE trial.[108] In March 2010, SynCardia received CE mark approval to market the Freedom driver in the European Union for use with the SynCardia TAH-t.[121]

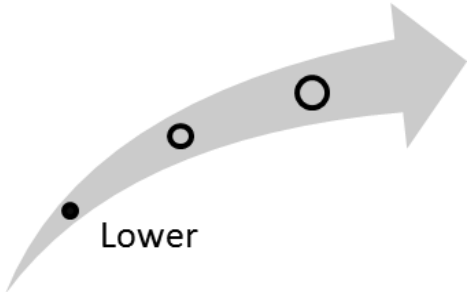
Diffusion and cost: The company reported that as of May 2014, about 1,300 SynCardia TAH-t devices had been implanted worldwide, and a subset of these (86 noted above) used the Freedom driver.[114] In the United States, the driver is available only through the IDE trial or under compassionate use at this time.

Costs for the Freedom Driver System have not yet been reported in the United States. Total cost of care for patients with artificial hearts using the portable driver at home presumably would be lower than that of hospitalized patients with artificial hearts, because the inpatient stay is shortened. However, the change in care setting may result in more of a cost shift than a significant cost reduction. Ambulatory patients would continue to need regular visits from specially trained nurses at home as well as followup office visits with specialist physicians to monitor device function. Furthermore, as with hospital-based pneumatic drivers, home use of the portable driver would require the immediate availability of a backup driver in case the primary unit fails and that someone (e.g., family member) be available to assist the patient. Thus, driver acquisition and maintenance costs are likely to be comparable for portable and hospital-based drivers. The majority of the overall treatment costs for these patients will continue to include the costs of the artificial heart itself and surgical implantation, regardless of whether patients are supported in the hospital with a conventional driver or at home with a portable driver. The following available cost information is based on inpatient use of the SynCardia TAH-t. Reported costs for a SynCardia TAH-t kit are approximately $124,700, which includes a patient simulator (for training), tubing, and surgical disposables in addition to the device itself.[122] Staff training costs to meet manufacturer's device-related certification requirements are approximately $98,000, plus $58,590 for a new center startup kit, in addition to device costs. SynCardia will loan a hospital the necessary driver units if the center remains certified to implant the TAH-t and maintains an inventory of two TAH-t kits and a spare kit.[122] Annual maintenance costs for the TAH-t are estimated at $18,000.[123,124] Additional costs related to inpatient care of patients in whom the TAH-t has been implanted include those for ancillary services, such as operating room use and attendant overhead; surgical team fees; charges for clinical staff; radiology, laboratory, and intensive care unit services; blood products; drugs; rehabilitation; and other professional payments.

Clinical Pathway at Point of This Intervention

American College of Cardiology Foundation/AHA clinical guidelines identify ventricular assist device implantation and cardiac transplantation as the only established surgical treatments for end-stage heart failure.[125] The portable driver system is intended to complement TAH-t use.[108] As a bridge to transplantation, the TAH-t with the Freedom driver would complement heart transplantation. Some left ventricular assist devices that are compatible with portable driver systems for in-home use could compete with the TAH-t and Freedom driver as a bridge to transplantation.

Figure 4. Overall high-impact potential: Portable Freedom Driver for in-home support of the temporary Total Artificial Heart



Although the intended patient population for this device is few in number, the portable Freedom Driver system has the potential to dramatically improve patient quality of life while awaiting a transplant and to dramatically shift the care setting from inpatient to outpatient, experts commenting on this intervention agreed. Experts also thought that this device has potential to reduce costs associated with lengthy hospital stays, although its outpatient use would require resources, such as training for staff and home caregivers/family members. Based on this input, our overall assessment is that this intervention is in the lower end of the high-impact-potential range.

Results and Discussion of Comments

Six experts, with clinical, research, and health systems backgrounds, offered perspectives on this intervention.[126-131] One of these experts declared a potential COI, because the expert is an active investigator in a trial studying a portable ventricular assist device, a possible competitor.[126] This potential COI is balanced by the perspectives of other experts who reported having no COIs. We have organized the following discussion of expert comments according to the parameters on which experts commented.

Unmet need and health outcomes: Although experts noted that the intended patient population for this device is small, they generally agreed that an important unmet need exists for a driver system that would allow patients to be discharged home while awaiting a heart transplant. Experts viewed this device's greatest potential benefits to be improving patient quality of life and decreasing costs of care by enabling patients awaiting a heart transplant to be discharged to home.

Use of this device could provide psychological benefits (increased independence, mobility, and quality of life), the experts generally thought. Some experts suggested a further health benefit might be realized by reducing risk of health care-acquired infection by getting patients out of the inpatient hospital setting. Some experts likened this technology's potential to that of ventilators and ventricular assist devices, which have migrated from inpatient care to outpatient care and a home setting with positive results.

Acceptance and adoption: If good outcomes are demonstrated from the ongoing trial, both clinicians and patients would readily adopt this technology because of its potential for lower costs and improved quality of life and health status, the experts thought. Although several experts also noted that extensive training (on the part of both hospital staff and patients' home caregivers) would be required for diffusion of this device, they did not think this would be a barrier to uptake.

Health care delivery infrastructure and patient management: Experts noted that shifting care from an inpatient setting to the home is important and would likely lower costs significantly, given the expense of continuous, long-term inpatient care. However, some experts anticipated that moving these patients home may simply shift costs and would increase the need for home-care personnel with experience in caring for patients who have received artificial hearts.

One expert representing a research perspective opined, "Ambulatory patients would continue to need regular visits from specially trained nurses at home as well as follow-up office visits with specialist physicians to monitor device function. Furthermore home use of the portable driver would require the immediate availability of someone (e.g., family member) be available to assist the patient."[128]

Health disparities: Experts generally agreed that the portable Freedom driver is likely to have minimal effect on health disparities. Some experts thought cost would have a potential impact on health disparities. One clinical expert opined, "This will be very costly and will have all the issues related to insurance status disparities."[126]

Valve and Structural Disorder Interventions

Transcatheter Aortic Valve Implantation (CoreValve) for Treatment of Severe Aortic Stenosis

Unmet need: In the United States, about 29% of people aged 65 years or older and 37% of people aged 75 years or older have aortic sclerosis, a precursor condition to aortic stenosis. However, degenerative calcific aortic stenosis, which usually manifests after age 75 years, is evident in only 2% to 9% of the elderly population.[132] Until approval of the first transcatheter aortic valve in the United States in 2011, the gold standard for treating severe aortic stenosis had been open surgical replacement of the valve with a mechanical valve or a bioprosthetic valve.[133-135] However, open-heart surgery is typically not an option for some patients—those who cannot withstand open surgery or who are at high risk of developing surgical complications.[133,134,136] Medical therapy has typically been the only therapeutic option for these patients; however, medical therapy is often ineffective in this population, and mortality tends to be high.[137-139] Thus, many patients live with aortic valve insufficiency, which compromises quality of life. Transcatheter aortic valve implantation (TAVI) with the CoreValve® System is the second approved transcatheter aortic valve that provides a minimally invasive therapeutic option for treating or delaying end-stage HF due to aortic stenosis in patients at high risk of complications from open surgical valve replacement.[140] The valve differs somewhat from the previously approved valve by another manufacturer in terms of sizes and design.

Intervention: This catheter-based valve implantation technology allows clinicians to implant the valve in a diseased aortic valve using minimally invasive techniques. TAVI, also known as transcatheter aortic valve replacement or TAVR, is intended to provide the therapeutic benefit of surgical aortic valve implantation to patients who are ineligible for surgery or at high risk of surgical complications.[134,136,141-143] The CoreValve System is composed of a porcine pericardial tissue valve mounted in a self-expanding, hourglass-shaped, nitinol-alloy mesh frame. The bioprosthetic valve is deployed using an 18 French diameter delivery catheter with a set of disposable catheter-loading components.[144-146]

The manufacturer states that typical implantation procedures last about 1–3 hours with the patient under sedation. The procedure is performed in a hybrid operating room with a multidisciplinary team that includes an interventional cardiologist and cardiac surgeon. Typically, the clinician guides a catheter into the heart through the femoral artery (unless another approach is deemed to be better for the patient, as discussed below), then threads a balloon catheter through the guide catheter into the heart. Once the balloon is positioned in the aortic valve, it is inflated to prepare for implanting the CoreValve. Using imaging equipment to direct placement, the clinician positions the CoreValve over the diseased aortic valve; in some cases, the diseased valve is removed before the CoreValve is placed. After placement, the catheter is withdrawn, and the incision is closed. The manufacturer states that the typical hospital stay after a TAVI procedure is 3–5 days.[147] One of three other, more-direct access routes can be used when the transfemoral route is impractical or undesirable because of severe, systemic vascular disease that impedes catheter navigation from the femoral artery. In the transapical approach, the physician makes a small incision between the ribs to access the heart apex (bottom) and advances the delivery catheter through the apex into the left ventricle to reach the aortic valve.[148,149] In the subclavian approach, the physician inserts a catheter under the clavicle into the subclavian artery to deploy the aortic valve.[147] Finally, the transaortic approach allows a physician to insert the delivery catheter into the aorta through the ribs using either a mini-thoracotomy in the second intercostal space or an upper hemisternotomy.[150,151] Valve deployment via alternate access routes is similar to that used in the transfemoral approach, once the delivery catheter is positioned.

Clinical trials: In March 2014, Adams and colleagues published clinical experience with CoreValve TAVI procedures in 795 patients with severe aortic stenosis at increased surgical risk. Investigators reported significantly lower 1-year mortality with TAVI than with open valve replacement surgery (14.2% vs. 19.2%). The authors also reported a reduced incidence of major cardiovascular and cerebrovascular events with no increase in the risk of stroke.[152]

In May 2013, the manufacturer reported 1-year results from the CoreValve ADVANCE International Post Market Study that suggested TAVI had low rates of mortality and stroke and improved hemodynamics (blood flow) in patients with severe aortic stenosis considered to be at high risk of surgical complications.[153] This study is a prospective, observational study intended to evaluate CoreValve TAVI procedures in patients outside of a clinical trial setting. Among the 996 treated patients overall, investigators reported on 806 of 824 patients (97.8%) for whom 1-year followup data were available. At 1 year, all-cause mortality was 17.9%; cardiovascular mortality was 11.7%; and the combined stroke rate was 4.5% (2.3% minor stroke rate and 2.3% major stroke rate). Investigators also observed substantial improvement in disease symptoms, as measured by the New York Heart Association (NYHA) scale of functional limitations due to heart failure. This scale has four major classifications, from I to IV; lower classifications indicate better health. At baseline, only 20% of patients were classified as NYHA class I or II. However, 30 days after TAVI, 85% of patients were classified as NYHA class I or II and, at 1 year, 87% of patients were classified as NYHA class I or II.[153]

Manufacturer and regulatory status: Medtronic, Inc. (Minneapolis, MN) manufactures the CoreValve System. The newest valve addition to its system is the CoreValve Evolut, a 23 mm valve that can fit an aortic annulus size of 18 mm. The CoreValve System now has four valve sizes (23, 26, 29, and 31 mm) to fit aortic annulus sizes that range from 18 to 29 mm.[154]

FDA granted Medtronic an investigational device exemption for its U.S.-based CoreValve trial in October 2010.[155] In October 2013, after the announcement of positive pivotal trial data, FDA announced that it would no longer require an advisory panel to consider the premarket approval application submission, and on January 17, 2014, FDA granted marketing approval for the CoreValve system to treat severe aortic stenosis in patients ineligible for surgical valve replacement.[156] FDA documentation indicates that the approval covers the entire CoreValve platform, including the 23 mm CoreValve Evolut and the CoreValve 26, 29, and 31 mm valves. Labeling information states that "patients must present with femoral or subclavian/axillary access vessel diameters of ≥6 mm or an ascending aortic (direct aortic) access site ≥60 mm from the basal plane."[156-158]

In Europe, CoreValve and CoreValve Evolut have the CE mark allowing marketing there, with the first European approval in May 2007. It is indicated for treating patients with severe aortic stenosis at high risk of surgical complications for use with the transfemoral, subclavian, and direct aortic delivery approaches,.[153,156]

A patent infringement suit had been brought against Medtronic by Edwards Lifesciences Corp. (Irvine, CA).[159] In January 2014, the court awarded Edwards Lifesciences a $392 million judgment and Edwards Lifesciences stated its intention to seek an injunction to prevent Medtronic from selling the CoreValve in the United States. However, the parties reached a settlement in May 2014 in which "all pending cases or appeals in courts and patent offices worldwide" were dismissed. The agreement "includes a provision that the parties will not litigate patent disputes with each other in the field of transcatheter valves for the eight-year duration of the agreement."[160]

Diffusion and cost: The reported cost of the CoreValve device is about $30,000,[161] similar to those of the Edwards Lifesciences's Sapien valve. Some research has suggested that overall treatment costs might be lower for patients receiving TAVI than open valve procedures. In November 2012, Reynolds and colleagues reported a cost-effectiveness comparison between TAVI

and open-heart aortic valve replacement among cohort A (high-risk) patients in the PARTNER trial.[162] The authors found that for transfemoral TAVI, procedural costs were substantially higher than those for open-heart aortic valve replacement ($34,863 vs. $14,451). However, overall treatment costs for the entire index hospitalization were somewhat lower for transfemoral TAVI than for open surgery ($71,955 vs. $74,452, p=0.53). The $2,497 cost reduction in favor of transfemoral TAVI compared with open valve surgery resulted from lower nonprocedural costs ($31,192 vs. $54,228), mainly because of a 6.2-day shorter length of stay in the transfemoral TAVI group (10.2 vs. 16.4 days, p<0.001).[162,163]

A cost-effectiveness analysis between transapical TAVI and open surgery showed transapical TAVI to have total index admission costs $11,008 higher than open surgical valve replacement ($90,548 vs. $79,540, p=0.08). Nonprocedural costs were $44,940 in the transapical TAVI group and $58,139 in the surgery group. Length of stay was reduced by 1.4 days in the transapical TAVI group compared with open surgery (14.7 vs. 16.1 days, p=0.39).[162,163]

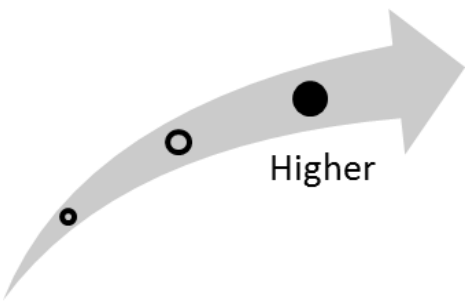
On May 1, 2012, CMS published a decision memo that outlines TAVR (acronym used by CMS) coverage under its Coverage with Evidence Development process.[164] CMS has established physician payments under its physician fee schedule. Inpatient procedures are generally reimbursed under various diagnosis-related groups already established for surgical valve replacement.[161,165,166] Under the decision memo, CMS provides TAVR coverage for treating symptomatic aortic valve stenosis for FDA-approved indications only when certain criteria are met.[164]

ECRI Institute routinely searches representative, private, third-party payers that publish their coverage policies online. A search showed the payers generally cover the procedure for patients who are not surgical candidates and that they have adopted requirements that are similar to or the same as CMS requirements; however, some payers have not followed suit and have not expanded coverage policies to include patients who are eligible for open surgery but at high risk of complications.[167-173]

Clinical Pathway at Point of This Intervention

Aortic valve replacement is considered the definitive surgical treatment of choice for most adults with severe aortic stenosis who are candidates for open heart surgery.[174,175] For patients who are not candidates for open surgery and have a poor prognosis, medical management or aortic balloon valvuloplasty were the only options. However, these options do not provide full relief of aortic stenosis symptoms.[133,134,176] The advent of TAVI provides a new option for patients with severe aortic stenosis who are not candidates for surgery or who are at high risk of surgical complications and would otherwise have no surgical treatment options.[136,177-179]

Figure 5. Overall high-impact potential: transcatheter aortic valve implantation (CoreValve) for treatment of severe aortic stenosis



Experts commenting on this intervention agreed that it offers an important new treatment modality for patients who have few options. However, one expert noted the availability of a similar

transcatheter heart valve. Experts opined that this intervention would improve patient health outcomes. However, one expert was concerned about the potential need for permanent pacemaker implantation after TAVI. Experts generally agreed that establishing a TAVI program requires significant infrastructure and staffing resources including capital and operational support. Experts agreed that the intervention has the potential for widespread acceptance by both patients and clinicians because of its less-invasive nature compared with open surgery. Based on this input, our overall assessment is that this intervention is in the higher end of the high-potential-impact range.

Results and Discussion of Comments

Five experts, with clinical, research, health systems, and health administration backgrounds, offered perspectives on the CoreValve technology.[180-184] Two of these experts declared potential COIs. One expert was a co-primary investigator of a clinical trial that studied a Medtronic device for treatment-resistant hypertension.[181] Another expert has received speaking honoraria from various competing manufacturers regarding electrophysiology interventions, but has not provided professional services regarding valve replacement.[180] The potential COIs are balanced by the perspectives of other experts who reported having no COIs. We have organized the following discussion of expert comments according to the parameters on which they commented.

Unmet need and health outcomes: The unmet need addressed by this intervention is extremely important, the experts concurred, citing the large number of patients who would be affected and the fact that effective options are very limited for this population. As one research expert stated, "For patients ineligible for open aortic valve surgery, TAVR is an appealing option since medical therapy is generally ineffective in these patients. For high risk surgical patients, TAVR may be worth the risk of intervention. Comparisons between low-risk surgical patients and TAVR are still needed to assess this population's potential benefit from TAVR."[183] This expert also commented that this patient population is growing as the U.S. population ages and as better techniques for identifying patients with aortic stenosis are developed.

Experts generally agreed on the potential of this intervention to significantly improve patient health outcomes, citing the relative low-risk procedure compared with surgical options and the inefficiency of pharmacotherapies. One clinical expert opined, "Patients who successfully undergo these procedures often have dramatic improvements in their symptoms and quality of life. These procedures also reduce mortality when compared with surgery or medical therapy."[181]

Acceptance and adoption: Clinicians who treat these patients would readily accept this technology, the experts thought, considering that no other interventions are available for this patient population. Experts also generally thought that patients would accept this procedure because it is considered to be minimally invasive. One expert representing a clinical perspective commented, "Patients almost always choose percutaneous versus surgical options - they want less done on them, less risk, less complications, shorter hospital stays."[180]

Health care delivery infrastructure and patient management: Experts generally agreed that TAVI has high potential to disrupt health care infrastructure and patient management. For centers who do not yet offer TAVI procedures, program implementation requires significant operational and capital support, one research expert opined.[182] Some experts commented that the need for training to perform TAVI has a substantial impact on health care delivery infrastructure. One clinical expert commented, "A whole team needs to be trained and in place—however, resources will likely shift from the surgical aortic valve team to the transcatheter one. It is not a big deal for centers that have a surgical team in place, but it will be a huge resource sink for those without one."[180]

Health disparities: Experts generally anticipated that TAVI would not alter health disparities significantly. Several experts listed high cost and limited availability of reimbursement as factors that would affect health disparities. One expert representing a research perspective commented that the high cost of TAVI coupled with inadequate reimbursement is limiting adoption by hospitals for fear of lost profits.[183] A clinical expert also commented regarding cost and reimbursement, "In theory, this procedure could save dramatically on health care costs by replacing a proportion of cardiac surgeries. However, currently the cost of the device is such that the procedure ends up being more expensive than surgery (from the hospital perspective, since reimbursement is not adequate at the present time)."[181]

Transcatheter Mitral Valve Repair (MitraClip) for Treatment of Mitral Regurgitation

Unmet need: Significant mitral regurgitation (MR) occurs in an estimated 1% to 2% (about 4 million) of the U.S. population. More than 250,000 cases of significant MR are diagnosed each year in the United States, and each year, about 50,000 people undergo some type of surgery for the disease.[185] Although surgical intervention (i.e., valve repair or replacement) is the preferred treatment for severe mitral regurgitation (MR), many patients are not candidates for these procedures because of a high surgical risk that stems from advanced age or extensive comorbidities.[186,187] Up to one-half of candidates with symptomatic, severe MR may not receive surgical intervention for this reason.[186] In light of this unmet need, investigators and manufacturers have developed less-invasive approaches to mitral valve repair. The MitraClip® Mitral Valve Repair System is a recently approved catheter-based approach to repairing the mitral valve that may offer a treatment option for patients at high risk for complications from surgery.[188]

Intervention: The MitraClip device is intended to simulate the functional effects achieved by the Alfieri edge-to-edge open surgical procedure used for treating MR.[187] In the Alfieri procedure, a surgeon sutures together the edges of the two opposing mitral valve leaflets at the center of the valve opening, leaving two smaller openings on either side that close more completely than a single large opening.[189] The MitraClip device mimics this procedure by "clipping together" the mitral valve leaflets, rather than using sutures.[187,190]

To implant the MitraClip, a physician inserts a guide catheter into the femoral vein at the patient's groin and threads it up to the heart into the right atrium under fluoroscopic guidance in a cardiac catheterization lab.[191] To reach the mitral valve in the left atrium, the physician performs a transseptal puncture to create an opening in the septum, the wall that separates the right and left atrial chambers, with the needle-like dilator within the catheter.[191,192] Use of transseptal atrial puncture, a difficult procedure, has traditionally been limited to large interventional cardiac care programs staffed with electrophysiologists who are well-experienced in the technique.[193]

As the procedure continues, the operator advances the catheter into the left atrium and through the mitral valve as the clip is expanded. Using Doppler ultrasound to assess the optimal clip placement, the physician grasps and fastens the edges of the valve leaflets together with the MitraClip.[191,192] Before releasing the implant from the clip delivery device for permanent placement, the physician confirms proper positioning with further ultrasound scans. If the device positioning is acceptable, the physician releases the clip from the delivery device and removes the catheter.[188,191]

The MitraClip device will most likely be used for patients with degenerative mitral valve disease with prolapse (backward collapse) originating mainly from the center of the valve, a fairly well-defined population that would not necessarily require additional types of cardiac intervention.[194,195]

Clinical trials: In 2013, Lim and colleagues published outcomes from 127 patients with severe, degenerative MR at a prohibitive risk for mitral valve surgery who were treated with MitraClip therapy. Investigators reported implantation success of 95.3% and a hospital stay of 2.9±3.1 days. Major adverse events reported at 30 days included death in 6.3%, stroke in 2.4%, and myocardial infarction in 0.8%. At 1 year, 30 patients (23.6%) had died, with no survival difference between patients discharged with primary or secondary MR.[196]

In 2013, investigators reported 1-year outcomes from 59 patients with severe, symptomatic MR and reduced ejection fraction who received MitraClip therapy.[197] The primary outcomes evaluated were procedural efficacy measured by reduction in MR and improvement in NYHA functional

classification. Investigators found that device implantation was associated with reduced MR and improved NYHA functional class, translating into improved 6-minute walk test distance. Followup echocardiography suggested a reversal in heart enlargement, with reduced left atrial volume and left ventricular end-systolic diameter and increased left ventricular ejection fraction (LVEF). These results were consistent with outcomes in a subgroup of 25 patients with severely reduced LVEF (ejection fraction 23±2%), suggesting that sicker patients also benefitted from MitraClip therapy. Investigators reported 30-day mortality of 2.9%.[197]

Also in 2013, investigators reported outcomes from 117 patients in the GRASP Registry.[198] The primary outcome measures were the rate of major adverse events at 30 days, freedom from death, surgery for mitral valve dysfunction, or grade 3+ or greater MR at 30 days and 1 year. Investigators reported acute procedural success, defined as residual MR grade 2+ or less after MitraClip implantation, in all patients and no procedure-related mortality. With experience, physicians substantially reduced their procedure times, although procedure times varied widely between cases involving implantation of a single clip and multiple clips. Major adverse events were reported for four patients at 30 days (4.3%). Thirteen patients experienced increased MR to MR grade 3+ or more at 1 year. At 1 year, no patients required surgery for mitral valve dysfunction. Freedom from death, freedom from surgery for mitral valve dysfunction, or freedom from grade 3+ or more MR was 96.4% at 30 days and 75.8% at 1 year.[198]

Manufacturer and regulatory status: The MitraClip is manufactured by the Abbott Vascular division of Abbott Laboratories (Abbott Park, IL). Abbott obtained the MitraClip technology through its acquisition of Evalve, Inc. (Menlo Park, CA), in November 2009.[199] In October 2013, FDA approved the device for treating patients who have received a diagnosis of "significant symptomatic degenerative MR who are at prohibitive risk for mitral valve surgery."[200]

MitraClip's approval process took several years to complete. Originally, the device was anticipated to be reviewed by FDA in 2011. In May 2011, the manufacturer issued a voluntary device recall—because of issues with the delivery catheter's tip—in Europe, Australia, Singapore, and other countries where the device had been approved. Although the company resolved the issue and reintroduced the device in those countries, the recall prompted FDA to request additional information and analysis regarding the MitraClip, which the company provided in an amended premarket approval application.[201]

The proposed indication for the MitraClip device was "the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥3+) in patients who have been determined by a cardiac surgeon to be too high risk for open mitral valve surgery and in whom existing co-morbidities would not preclude the expected benefit from correction of the mitral regurgitation."[202] In March 2013, the Circulatory System Devices Panel of FDA's Medical Devices Advisory Committee voted on three questions (safety, effectiveness, risk-benefit ratio) pertaining to the premarket approval application for Abbott's MitraClip system. The panel voted 5-3 that MitraClip's benefits outweigh the risks for use in patients who meet the criteria specified in the proposed indication. The panel voted 8-0 that available data "show reasonable assurance" that MitraClip implantation would be safe when used for the proposed indication. However, the panel voted 5-4, with the chairman voting as tie breaker, that available trial data did not provide "reasonable assurance" that the MitraClip procedure would be effective for its proposed indication.[203]

After the panel meeting, Abbott and FDA determined "that patients with primary MR etiology ([degenerative MR]) at prohibitive risk of surgery were the appropriate patient population to evaluate the risks and benefits of the MitraClip device." As opposed to functional MR, patients with degenerative MR are not amenable to medical therapy and, therefore, the subset of patients with degenerative who are at prohibitive surgical risk lacks effective treatment options. A retrospective study of patients with degenerative MR at prohibitive surgical risk was performed (see Lim et al.

2013)[196] and MitraClip's premarket approval application approval was based on this patient population.[202]

Diffusion and costs: In Europe, the MitraClip device's list price is approximately $26,200.[204] Hospitals reporting device costs to ECRI Institute's PriceGuide database reported a costs ranging from $25,000 to $30,000 for the Mitral valve kit (as of June 2014),[205] which concurs with prices reported from other sources.[206,207] Procedural costs to implant MitraClip might be somewhat higher than those of other interventions performed in a cardiac catheterization lab, such as percutaneous transluminal coronary angioplasty with stenting of the coronary arteries, because transseptal puncture is required to implant the MitraClip in the left heart. MitraClip therapy would be expected to substantially increase short-term treatment costs compared with medical management alone in patients who are ineligible for open mitral valve repair.

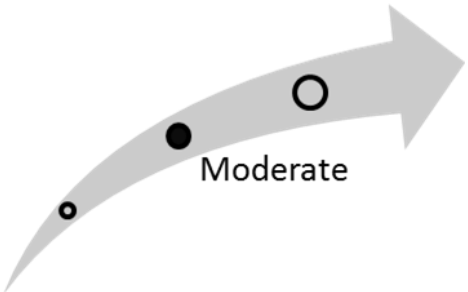
The device is just beginning to diffuse, given the recency of its approval. Its adoption may be slow initially because of safety alerts in 2013 and product recalls in 2011 that could affect physician and patient acceptance. The availability of reimbursement for the device and procedure also could affect physician acceptance and diffusion. Two representative, private, third-party payers (i.e., Humana, United Healthcare) consider MitraClip therapy investigational at this time and deny coverage for the procedure.[208,209]

Abbott requested a new technology add-on payment from CMS, but was denied, and reportedly stated intentions to make the request again, which if granted, would not take effect before October 2014 at the earliest.[207] CMS initiated a national coverage analysis (NCA) for transcatheter mitral valve procedures November 18, 2013.[210] On May 15, 2014, CMS issued a Proposed Decision Memo stating that it proposes to cover transcatheter mitral valve procedures under coverage with evidence development when certain criteria are met.[211] The NCA is expected to be completed by August 16, 2014.[210]

Clinical Pathway at Point of This Intervention

The preferred treatment for severe MR is open surgery for valve repair or replacement.[186,187] ACC/AHA clinical guidelines recommend surgical mitral repair over mitral valve replacement in most patients because the "valve is suitable for repair and appropriate surgical skill and expertise are available."[212] MitraClip may potentially be positioned as a catheter-based (transcatheter) alternative to surgical valve repair.[186,187]

Figure 6. Overall high-impact potential: transcatheter mitral valve repair (MitraClip) for treatment of mitral regurgitation



Overall, experts agreed this procedure addresses a considerable unmet need and has the potential to improve patient health. However, most experts opined that more data concerning safety and long-term outcomes are needed. Experts' opinions differed somewhat about how much this intervention would disrupt health care delivery for this condition. Some experts believe the disruption to health care delivery would be limited, because the infrastructure to perform the

procedure is already in place at many health care facilities offering valve surgery, although other experts believe that the potential increase in numbers of patients seeking treatment for functional MR has potential to cause a large disruption to health care delivery. The majority of experts thought the MitraClip would increase health care costs, but they wanted to see more long-term data to assess whether the device would reduce long-term costs of care for this patient population. Based on this input, our overall assessment is that this intervention is in the moderate high-impact-potential range.

Results and Discussion of Comments

Six experts, with clinical, research, health systems, and health administration backgrounds, offered perspectives on this technology.[213-218] We have organized the following discussion of expert comments according to the parameters on which they commented.

Unmet need and health outcomes: The unmet need for less-invasive interventions to treat MR is important, the majority of experts generally agreed, citing the large number of patients with MR who are not candidates for surgical repair and the ineffectiveness of pharmacotherapy. One expert with a health systems perspective noted that pharmacological treatments act as a "Band-Aid" instead of an effective cure.[218]

Experts generally agreed this intervention has potential to improve patient health outcomes, citing decreased mortality and morbidity in patients who are not good surgical candidates. However, several experts commented about the lack of randomized controlled trial data. One expert representing a research perspective commented, "Limited evidence suggests that MitraClip may be a reasonable option in patients who have no other good treatment options."[216]

Experts also expressed concerns about device and procedure safety and believe that the numerous comorbidities seen in these patients would present risk and preclude some patients from achieving greatly improved outcomes. One expert representing a research perspective opined, "Transseptal puncture required to access the left heart chambers is technically challenging and carries risk of life-threatening complications. Due to the complexity of procedure, the procedure would likely be performed in centers with established interventional cardiac programs."[215]

Acceptance and adoption: Although most experts agreed that the MitraClip implant would entail a significant learning curve and training for clinicians, they agreed that if clinical trial data continue to demonstrate benefits and safety, clinical acceptance would follow. Several experts listed the difficulty of the procedure and reimbursement to be potential barriers to clinician acceptance. One clinical expert commented, "This is a technically challenging procedure for multiple reasons: 1. Transseptal puncture - usually performed by electrophysiologists and less frequently by interventionalists so will need extra training. 2. Extra training on actual deployment of mitral clip - again not usually performed by interventionalists. However, given the potential number of patients who may meet criteria for this procedure, I believe that it will be embraced by clinicians."[217]

Experts generally agreed on the potential for wide patient acceptance of this intervention, citing the limited amount of treatment options and relatively less-invasive nature of the procedure compared to surgery.

Health care delivery infrastructure and patient management: Experts offered varied perspectives about this intervention's potential impact on the health care system. Some experts commented that little disruption to health care delivery would occur because the infrastructure is already in place, while other experts noted that the increase in case volume might cause a large disruption to health care delivery. One clinical expert stated that this intervention would likely only be offered in facilities that already have equipment and staffing in place to perform the procedure.[217] Conversely, some experts attributed the potential for disruption to significant training requirements.

The device and its related procedure would be expensive and affect overall health care costs, the experts generally agreed. The importance of long-term studies in determining overall impact on health care costs was noted by most experts. But a few experts thought that the MitraClip would affect health care costs only minimally, reasoning that this procedure would be less costly than surgical treatment or long-term care of patients who are not eligible for surgery.

Health disparities: Experts all agreed that this device would have minimal impact on health care disparities. However, several experts cited cost, reimbursement, and limited access to centers with established interventional cardiac programs to be potential factors that could affect health disparities.

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